46. (New) The method according to claim 44, wherein the promoter element is not operably linked to a repressor region of a $GABA_B$ receptor 1 P1b promoter.

47. (New) The method according to claim 46, wherein the promoter element further comprises:

(i) the nucleic acid sequence of positions 4080-4087 of SEQ ID NO: 2;

(ii) the nucleic acid sequence of positions 4196-4204 of SEQ ID NO: 2;

(iii) the nucleic acid sequence of positions 4241-4249 of SEQ ID NO: 2; and

(iv) the nucleic acid sequence of positions 4272-4279 of SEQ ID NO: 2.

REMARKS

I. Amendment of the claims

Upon entry of this Amendment, *currently-considered* claims 32-41 remain pending and new claims 42-47 are pending pursuant to the withdrawal of the finality of the outstanding Office Action, as requested in Section III. below. Applicants further note that the total number of claims pending in the application

is not changed by the addition of new claims 42-47 herein, since claims 22-27 have been cancelled.

Support for new claims 42 and 43 is found in Figure 4; page 14, lines 5-8; and page 19, lines 16-18 of the originally filed application. Support for new claims 44-47 is found in Figure 4; page 14, lines 5-8; page 19, lines 26-31; page 22, lines 1-17; and the Sequence Listing entry for SEQ ID NO: 2 of the originally filed application.

Independent claims 32 and 37 are each amended herein to delete two of the elements of the Markush group recited in each claim. Claims 22-27 are canceled herein without prejudice. Applicants expressly reserve the right to later claim and prosecute the subject matter deleted as a result of canceling claims 22-27 and amending claims 32 and 37 herein.

Claims 1-21 and 28-31 are pending and remain withdrawn from consideration.

No new matter is added by any of the amendments of the claims herein.

II. Drawings of the instant application

Applicants learned for the first time, as a result of the Office Action mailed August 13, 2002, that the 6 sheets of originally filed drawings (Figures 1-6) were apparently lost in the Patent Office and were not considered by the Examiner in any

prior examination of the application or Applicants' responses to previously issued Office Actions. A copy of Applicants' return postcard indicating the submission of the 6 sheets of drawings and stamped by the Patent Office to indicate the August 22, 2000 receipt of the application materials is enclosed as evidence of Applicants' original filing of the drawings.

In view of the above, enclosed herewith is a complete set of Figures 1-6 as originally filed in the instant application, the consideration of which Figures is hereby requested.

III. Request for withdrawal of finality of Office Action

In view of the Examiner not having been able to fully consider the application in his examination due to the loss of the originally filed drawings, Applicants request the withdrawal of the finality of the Office Action mailed August 18, 2002.

IV. Objection to the specification under 37 C.F.R. §1.81

The specification is objected to under 37 C.F.R. §1.81 for the omission of drawings. (Office Action, page 2, ¶3.) In view of Section II. above, Applicants request the withdrawal of the present objection.

V. Claim rejections under 35 U.S.C. §112, first paragraph: enablement requirement

(A.) Claims 22-27 and 32-41 are rejected under 35 U.S.C. §112, first paragraph, "scope of enablement," for the reasons alleged on pages 3-4 of the Office Action mailed March 12, 2002. (Present Office Action, page 3, lines 1-19.) Specifically, the Examiner asserts that the application is not enabled for "functionally equivalent modified forms" and "active fragments" of the subject $GABA_B$ receptor 1 promoters, nor for the allegedly "excessive" number of promoters hybridizing to the complement of SEQ ID NO: 1 or SEQ ID NO: 2.

With respect to claims 22-27, the rejection has been rendered moot by the cancellation of these claims herein.

With respect to claims 32-36, the claims do not recite "functionally equivalent modified forms" and "active fragments" and, as amended herein, the Markush group elements of independent claim 32 which were directed to hybridization have been deleted, without prejudice. Therefore, pursuant to this Amendment, withdrawal of the present reject of claims 32-36 is requested.

With respect to claims 37-41, the Examiner is respectfully directed to consider originally filed Figures 4 and 5 and Applicants' prior submitted arguments showing that the originally filed application discloses numerous actual examples

of functionally equivalent modified forms and active fragments of the subject promoters. Specifically, Applicants note that Figure 4 shows four P1a promoter fragments having substantial activity over a negative control and six P1b promoter fragments having substantial activity over a negative control. Further, Figure 5 shows seven functionally equivalent modified forms of the P1a promoter and eleven functionally equivalent modified forms of the P1b promoter. In addition, independent claim 37 has been amended herein, without prejudice, to delete the Markush group elements which were directed to hybridization.

In view of the above, withdrawal of the present rejection of claims 37-41 is also requested.

(B.) Claims 22-27 and 32-41 are rejected under 35 U.S.C. §112, "scope of enablement," for allegedly being of excessive breadth since Applicants have allegedly only disclosed two promoters, i.e., SEQ ID NO: 1 and SEQ ID NO: 2, yet "under the most stringent conditions, hundreds of DNA molecules may hybridize to these promoters." (Office Action, page 3, line 19-28.)

With respect to claims 22-27, the rejection has been rendered moot by the cancellation of these claims herein.

With respect to claims 32-41, the present rejections are rendered moot since the Markush group elements which recited

hybridization have been deleted as a result of amending independent claims 32 and 37 herein.

In view of the above, Applicants request withdrawal of the present claims rejection under 35 U.S.C. §112, first paragraph for alleged lack of enablement.

VI. Claim rejections under 35 U.S.C. §112, first paragraph: written description requirement

Claims 22-27 are rejected under 35 U.S.C. §112, first paragraph for allegedly not satisfying the written description requirement, for the reason provided on pages 4 and 5 of the Office Action mailed March 12, 2002. (Present Office Action, page 4, lines 1-19.)

The present rejection has been rendered moot by the cancellation of claims 22-27, without prejudice, herein.

VII. Claim rejections under 35 U.S.C. §112, second paragraph

Claims 23-27 are rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness for the reasons provided on page 5 of the Office Action mailed March 12, 2002. (Present Office Action, page 4, lines 20-25.)

The present rejection has been rendered moot by the cancellation of claims 23-27, without prejudice, herein.

MARKED-UP VERSION SHOWING REVISIONS TO CLAIMS

32. (Amended) A method for screening compounds for modulation of $GABA_B$ receptor 1 transcription, comprising the steps of:

(a) providing a host cell hosting an expression system comprising a nucleic acid molecule constituting:

a promoter element selected from the group consisting of:

(i) a nucleic acid molecule comprising SEQ ID NO: 1,

[(ii) a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence complementary to SEQ ID NO: 1 under conditions at least as stringent as those provided by performing a hybridization to filter-bound DNA at 65° C in a buffer consisting of 0.5M $NaPO_4$, 7% sodium dodecyl sulfate, 1mM EDTA followed by a washing at 68° C in 0.1X SSC buffer containing 0.1% sodium dodecyl sulfate,]

(ii) [(iii)] a nucleic acid molecule at least 95% homologous to SEQ ID NO: 1,

(iii) [(iv)] a nucleic acid molecule comprising SEQ ID NO: 2, and

[(v) a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing, under stringent conditions to a nucleotide sequence complementary to SEQ ID NO: 2, at least as stringent as those provided by performing a hybridization to filter-bound DNA at 65° C in a buffer consisting of 0.5M $NaPO_4$, 7% sodium dodecyl sulfate, 1mM EDTA followed by a washing at 68° C in 0.1X SSC buffer containing 0.1% sodium dodecyl sulfate, and]

(iv) [(vi)] a nucleic acid molecule at least 95% homologous to SEQ ID NO: 2; and

a reporter gene, wherein the promoter element is coupled to the reporter gene so that expression of the reporter gene is under the control of the promoter element;

(b) contacting a test compound with the cell; and

(c) determining whether the test compound modulates the level of expression of the reporter gene.

37. (Amended) A method for screening compounds for modulation of $GABA_B$ receptor 1 transcription, comprising the steps of:

(a) providing a host cell hosting an expression system comprising a nucleic acid molecule constituting:

a promoter element consisting essentially of a functionally equivalent modified form or active fragment of a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecule comprising SEQ ID NO: 1,

[(ii) a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence complementary to SEQ ID NO: 1 under conditions at least as stringent as those provided by performing a hybridization to filter-bound DNA at 65° C in a buffer consisting of 0.5M $NaPO_4$, 7% sodium dodecyl sulfate, 1mM EDTA followed by a washing at 68° C in 0.1X SSC buffer containing 0.1% sodium dodecyl sulfate,]

(ii) [(iii)] a nucleic acid molecule at least 95% homologous to SEQ ID NO: 1,

(iii) [(iv)] a nucleic acid molecule comprising SEQ ID NO: 2, and

[(v) a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing, under stringent conditions to a nucleotide sequence complementary to SEQ ID NO: 2, at least as stringent as those provided by performing a hybridization to filter-bound DNA at 65° C in a buffer consisting of 0.5M $NaPO_4$, 7% sodium dodecyl sulfate, 1mM EDTA followed by a washing at 68° C in 0.1X SSC buffer containing 0.1% sodium dodecyl sulfate, and]

(iv) [(vi)] a nucleic acid molecule at least 95% homologous to SEQ ID NO: 2; and

a reporter gene, wherein the promoter element is coupled to the reporter gene so that expression of the reporter gene is under the control of the promoter element;

(b) contacting a test compound with the cell; and

(c) determining whether the test compound modulates the level of expression of the reporter gene.

CONCLUSION

Applicants have completely responded to the Office Action. The Assistant Commissioner is hereby authorized to charge any fee due in connection with this communication to Deposit Account No. 23-1703.

Dated: February 13, 2003

Respectfully submitted,

Paul Diamond
Reg. No. 48,532
Agent for Applicants

Customer No. 007470
Agent's Dir. Line: (212) 819-8425

Enclosures

1. copy of originally filed Figures 1-6 (6 sheets)
2. copy of return postcard for application filing of August 22, 2000

EXPRESS MAIL NO.: EL 286876132US

Date 08/22/00

Assistant Commissioner for Patents
Box PCT
Washington, D.C. 20231

09/622745

Atty. Docket 1103326-0633

Serial No. TBA

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Kindly acknowledge receipt of the accompanying 1 pg abstract, 1 pg listing

- ☒ Specification and Claims 31 532 Rec'd PCT/PTO 22 AUG 2000 pages,
- ☒ ~~Oathor~~ Declaration and Power of Attorney ☒ Executed ☐ ~~Not Executed~~
- ☒ 6 Sheets of ~~formal~~ ~~informal~~ drawings
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